

AMENDMENTS TO THE SPECIFICATION:

(a) Please associate the attached sequence listing, presented in both paper and computer readable format, with this application.

(b) Please replace the paragraph beginning at page 1, line 1, with the following:

This is a division of Application No. 09/632,974, filed August 4, 2000, ~~(allowed)~~
now United States Patent No. 6,670,455 B1. ~~claiming benefit~~ The application also
claims priority to German Application No. 19937218.7, filed August 6, 1999. Both the
parent United States and German priority applications ~~, for which benefit of priority is~~
~~claimed herein, and both of which~~ are incorporated herein by reference.

(c) Please replace the paragraph at page 1, lines 9-26, with the following:

German patent application 19 903 693.4 has already disclosed a protease for the activation of blood clotting factor VII, a process for its production, for its detection and for its inactivation, and pharmaceutical preparations which contain this protease. This protease, first isolated from plasma, occurs there together with a nonactivated form, which is designated below as "proenzyme". The protease activates blood clotting factor VII and accelerates clotting, as was shown by numerous experiments. In the further investigation of the biological properties of this protein, identified as serine protease, it emerged that single-chain plasminogen activators, such as prourokinase, are also effectively activated. Moreover, inactivation of factors V and VIII in vitro was observed. In addition to the sequenced regions already described in German patent application 19 903 693.4, N-terminal sequencings of protease fractions were carried out. The following

amino acid sequences characterize the FVII-activating protease: IYGGFKSTAGKHP (SEQ ID NO:1); LLESLDPDXTPD (SEQ ID NO:2); EFHEQSFRVEKI (SEQ ID NO:3); SKFTXAXPXQFK (SEQ ID NO:4); where X means not identified. The sequences of the protease mentioned elucidated up to now show that they agree 100% with sequences of the protease published by Choi-Miura (Choi-Miura et al. J. Biochem. 1996; 119: 1157 to 1165).

(d) Please replace the paragraph at page 2, lines 1-11, with the following:

The investigations until now have especially concentrated on the protease in its activated form. The inactive form of the protease present in the plasma as a proenzyme was only recently discovered by means of a protein band pattern in the SDS-PAGE (sodium dodecyl sulfate – polyacrylamide gel electrophoresis) after reduction of the sample. Since, on the activation of the protease, a cleavage at a site of the primary structure typical for serine proteases and thus activation takes place, two or more bands are visible on electrophoresis. On reduction of the chains which are connected by disulfide bridges, the individual bands become visible in accordance with their lower molecular weight, the proenzyme remaining as a large individual chain. This was also clear in more complex solutions after transfer of the proteins to membranes and subsequent Western blotting using suitable antibodies.

(e) Please replace the paragraph at page 9, lines 13-22, with the following:

The eluate solution was used for further analysis. An SDS-PAGE with subsequent transfer to a PVDF (poly-vinylidene di-fluoride) membrane and detection of

the factor VII activator band was carried out using the unreduced and using the reduced sample. Activity tests of the proteins thus obtained were carried out according to the process described in German patent application 199 26 531.3, namely the activation of prourokinase and factor VII, with subsequent detection of urokinase or activated factor VII. The amounts of protease tested in this system, determined as protease antigen, correspond to the expected theoretical activity, whereby the activity of the isolated protease or of the proenzyme with respect to the biological activity was shown.